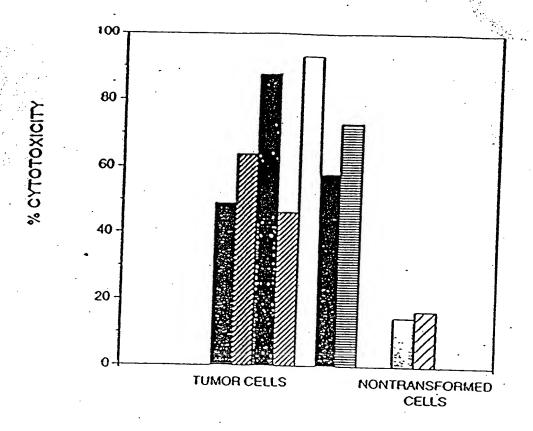


— SK-OV-3
— HEY
— OVCAR-3
— MOA-468
— A375-M
— HS294T
— A431

FIG. 1



- **⊠** 00001
- **Ø** SK-OV-3
- HEY
- OVCAR-3
- U JURKAT
- LANCAP
- **目** FTC
- O FS O HUVEC

FIG. 2

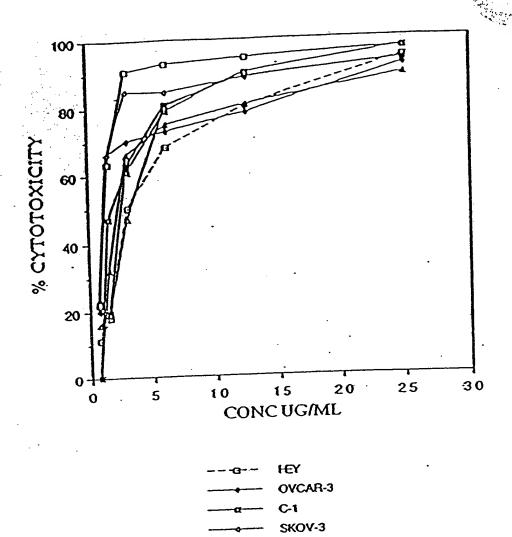
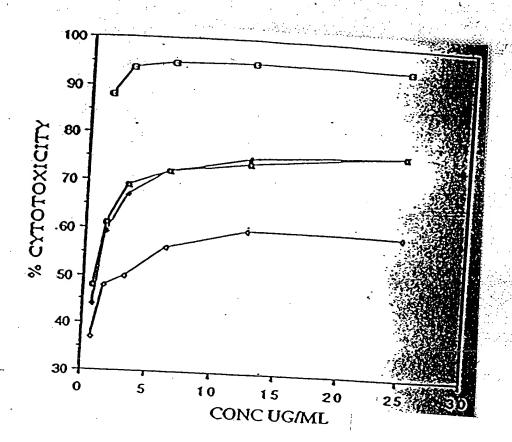


FIG. 3

PANC-1

A498



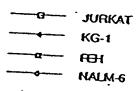
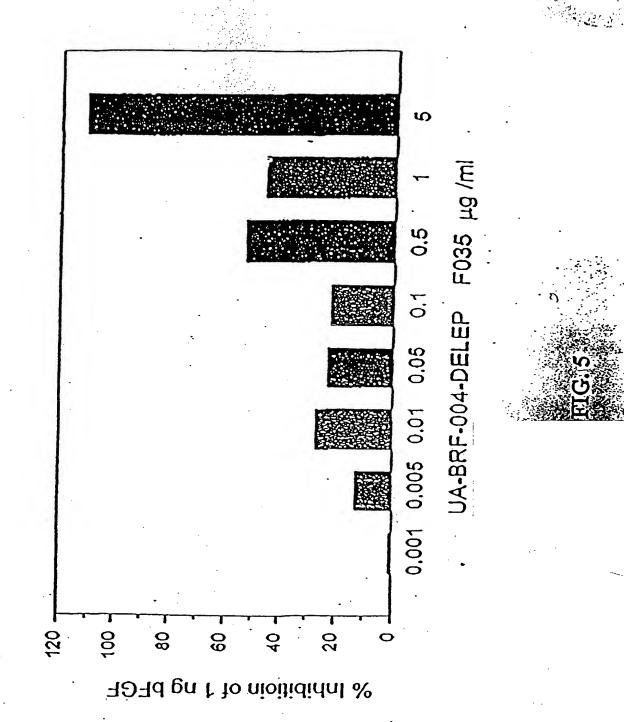
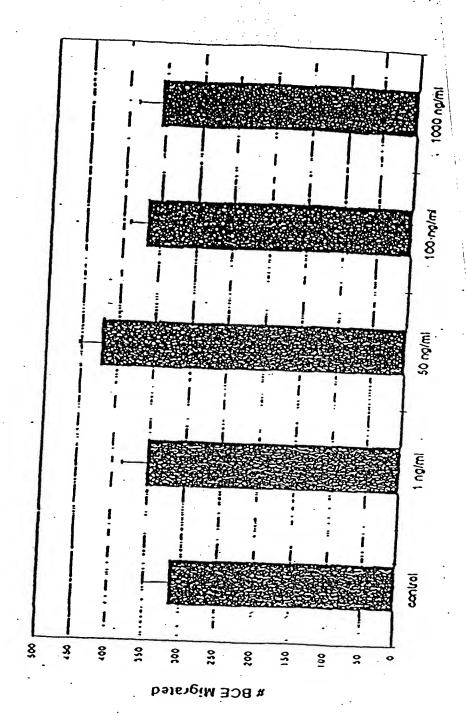


FIG. 4





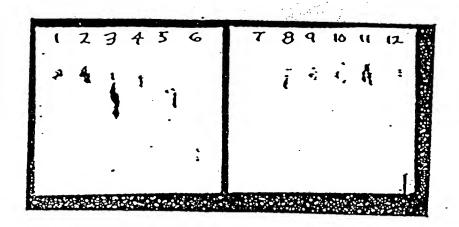


FIG. 7

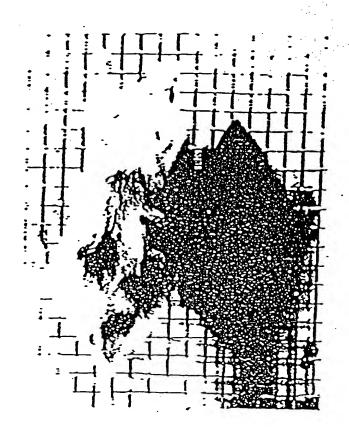


FIG. 8

Dose: 0.2 ml

ACETONE
4 weeks

Mouse # 13

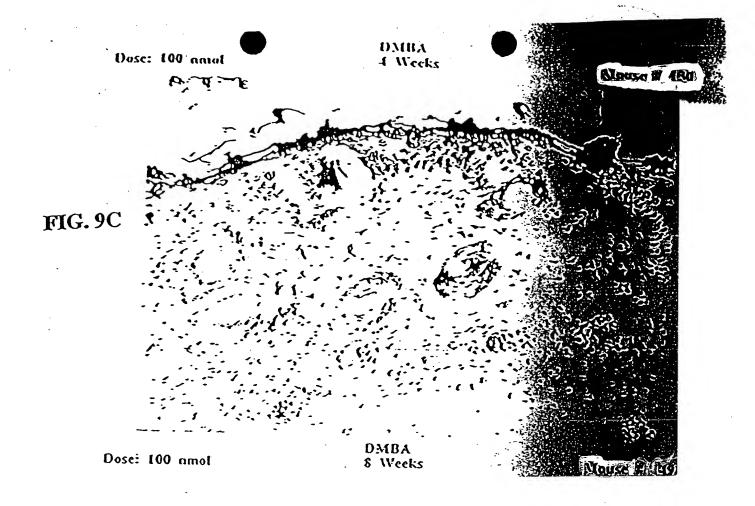
FIG. 9A

Dose: 0.2 ml

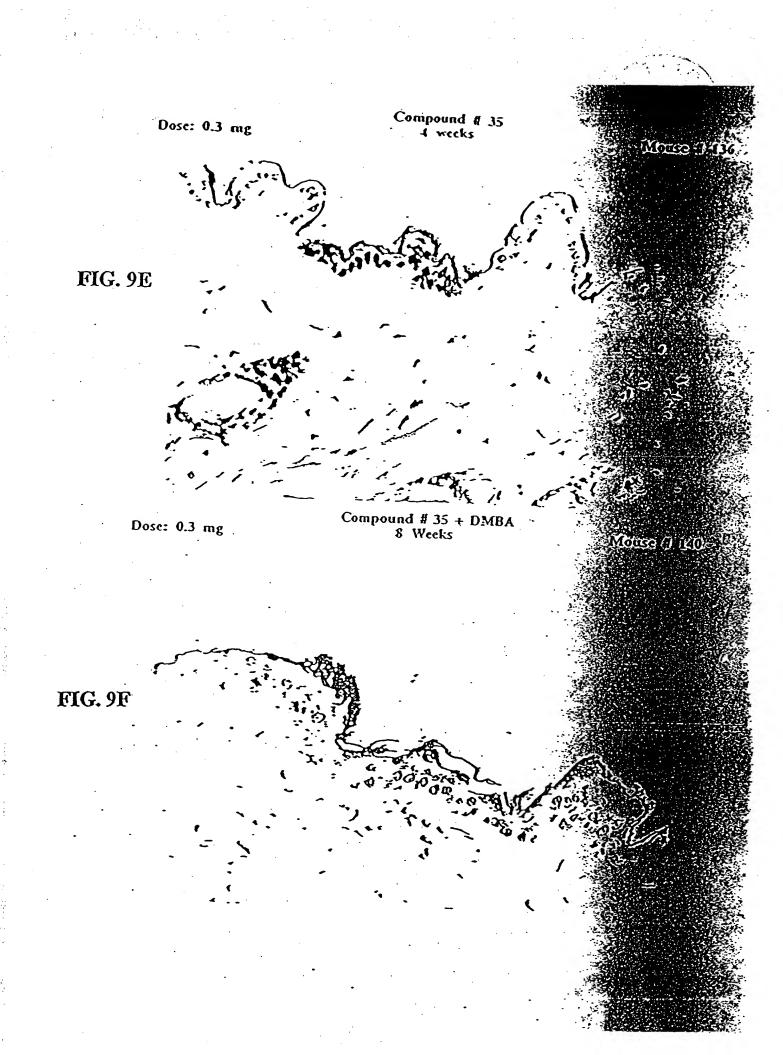
ACETONE 8 Weeks

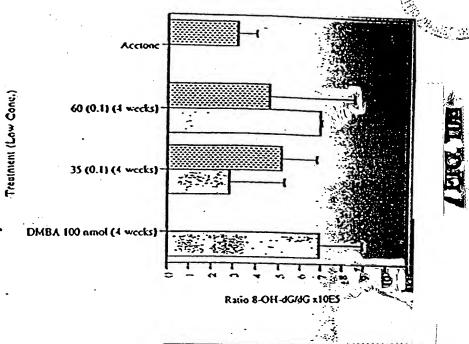
Mouse # 150

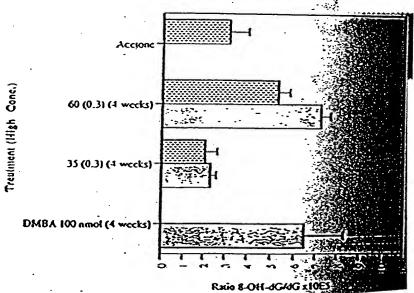
FIG. 9B





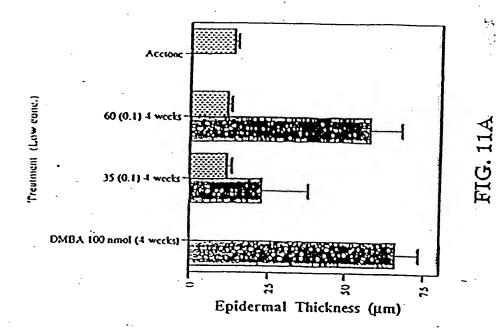


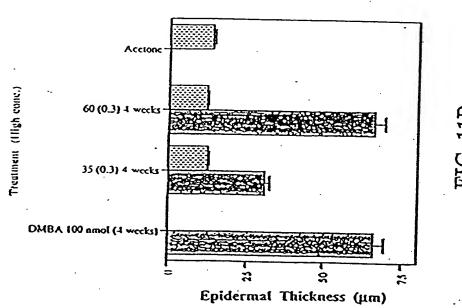




B DMBA

A8140.





🖾 - DMBA

B -DMBA

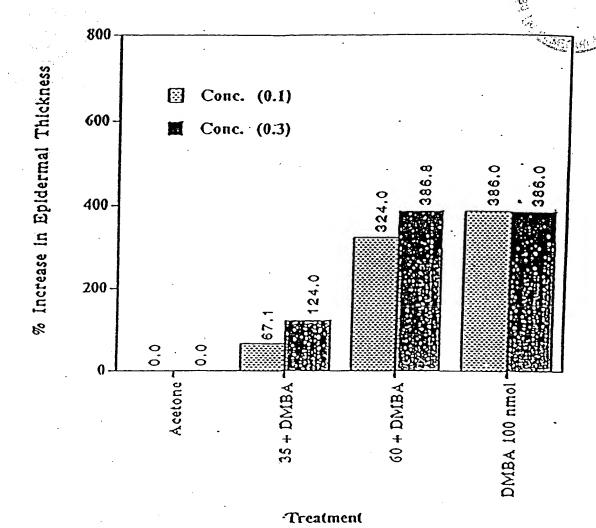


FIG. 12



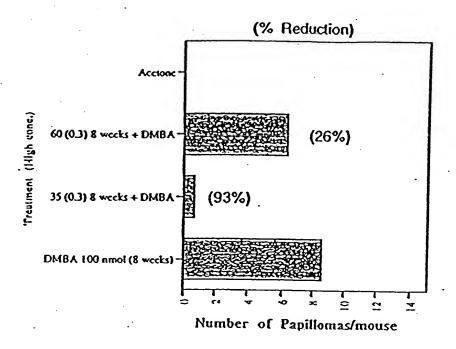


FIG. 13

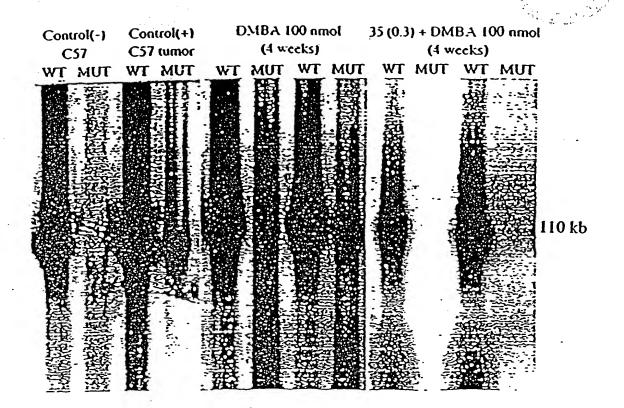


FIG. 14

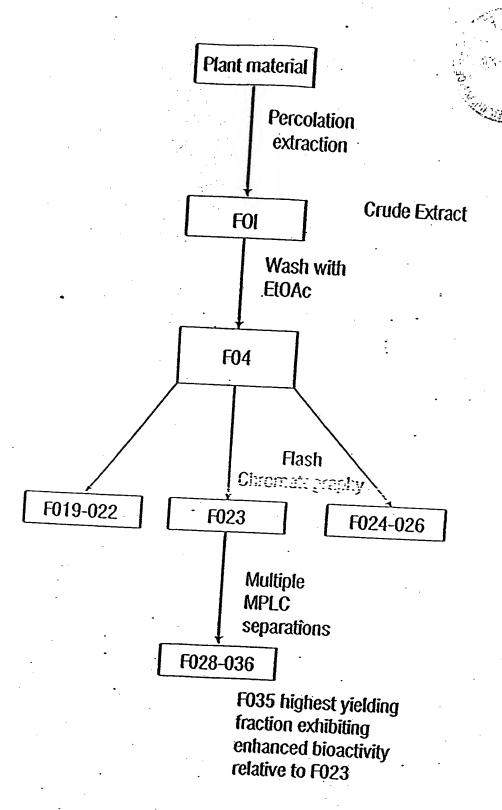


FIG. 15

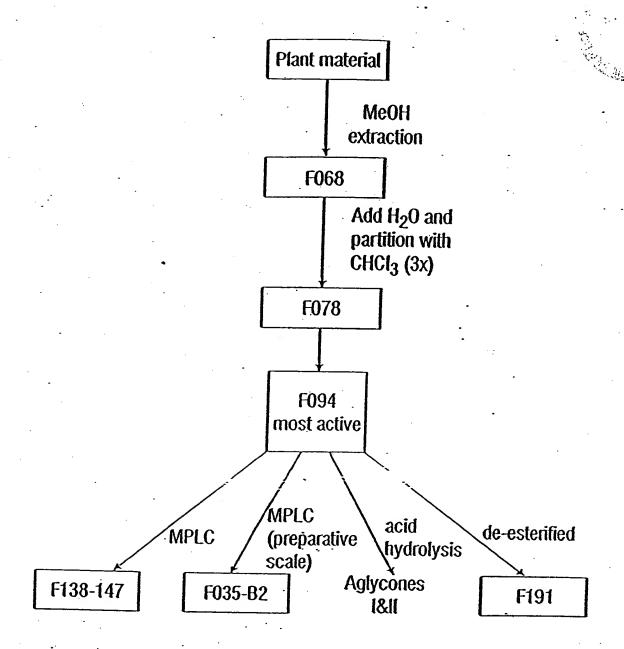


FIG. 16

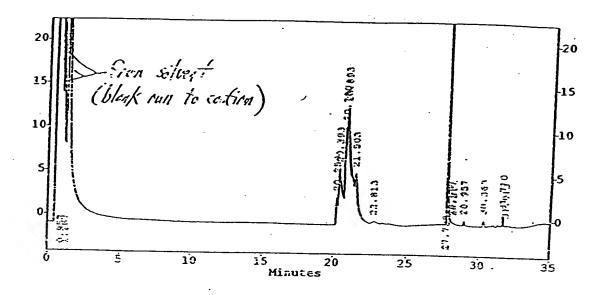


FIG. 17A

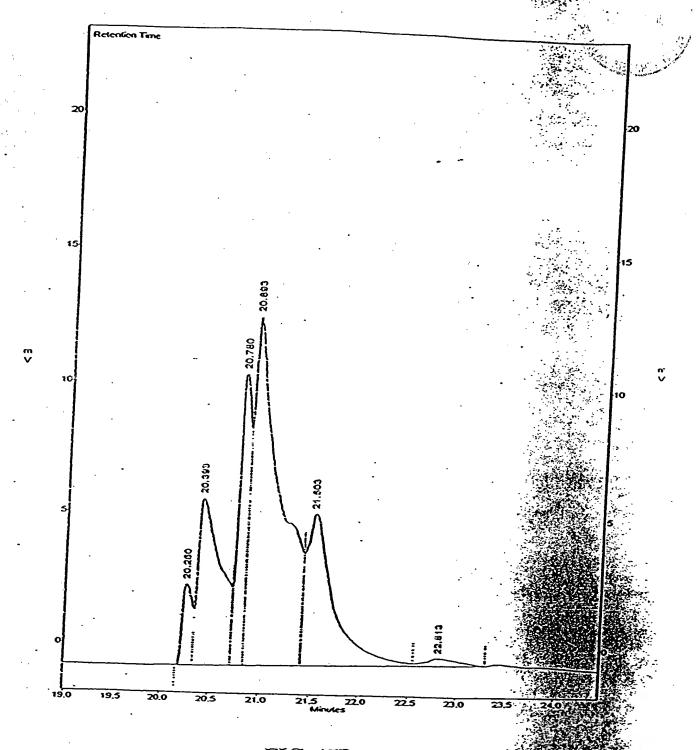


FIG. 17B

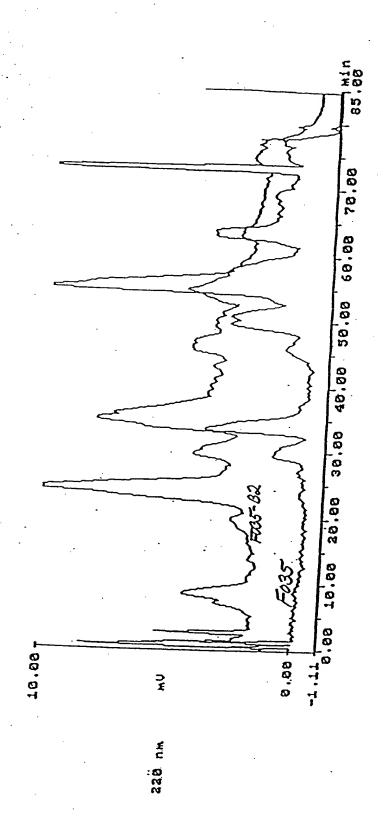


FIG. 18A

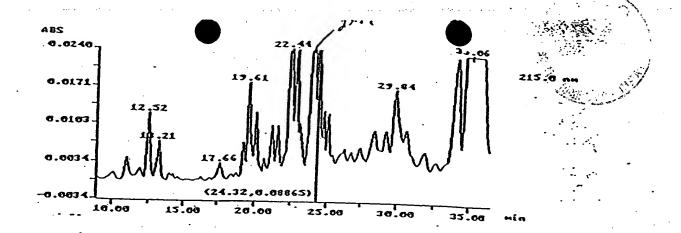


FIG. 18B

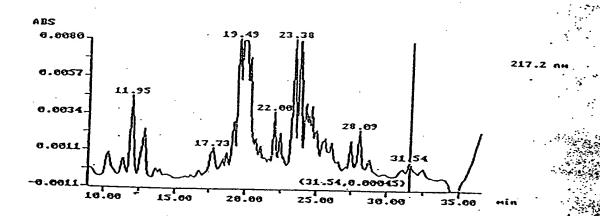


FIG. 18C

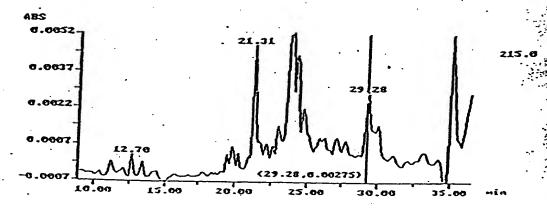


FIG. 18D

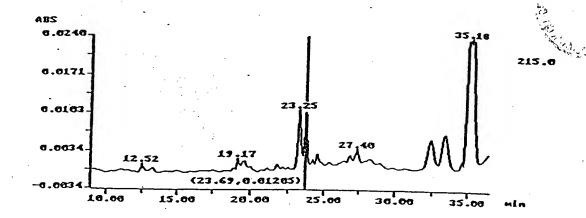


FIG. 18E

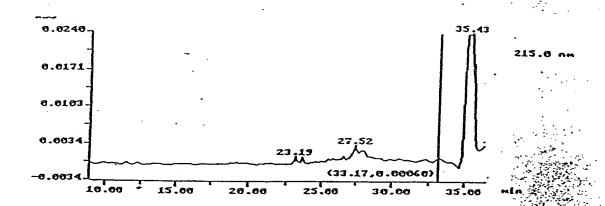
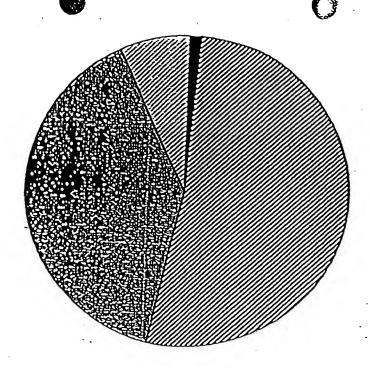


FIG. 18F



Sub G-0 (0.9%)
G-1 (47.9%)
S (36.1%)

G-2+M (6.8%)

FIG. 19A

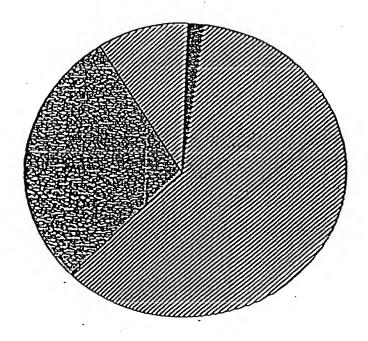


FIG. 19B

図 sub G-0 (1.6%) 図 G-1 (57.4%) 図 S (26.6%) ± 図 G-2+M (8.6%)



1 2 3 4 5 6 7 8 9 10 NF-κB—

- 1:Untreated
- 2:TNF (100pM)
- 3: F035 (1ug/ml)
- 4: TNF+ F035 (1ug/ml)
- $5 : F035 (2\mu g/ml)$
- 6: TNF+ F035 (2μg/ml)
- $7 : F094 (1 \mu g/ml)$
- $8: TNF+F094 (1\mu g/ml)$
- 9: F094 (2ug/ml)
- 10: TNF+ F094 (2ug/ml)

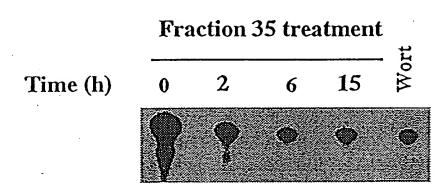


FIG 21

FIG 22

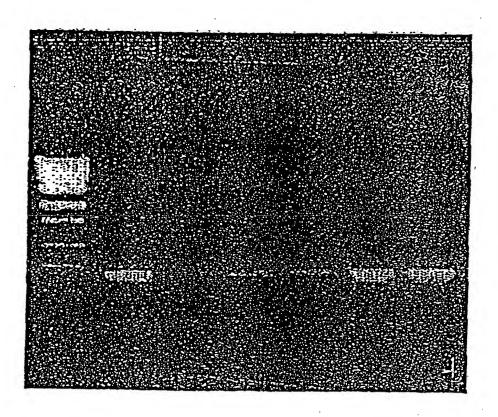
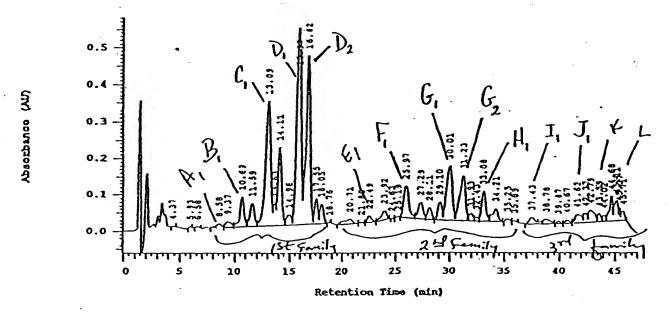


FIG 23

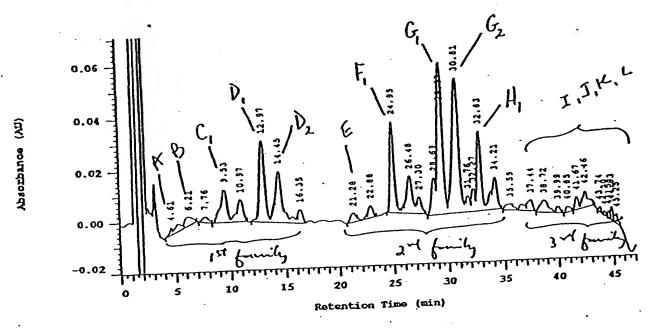
STRUCTURE OF ELLIPTOSIDES: ELLIPTOSIDE E if R=OH ELLIPTOSIDE A if R=H

FIG 24



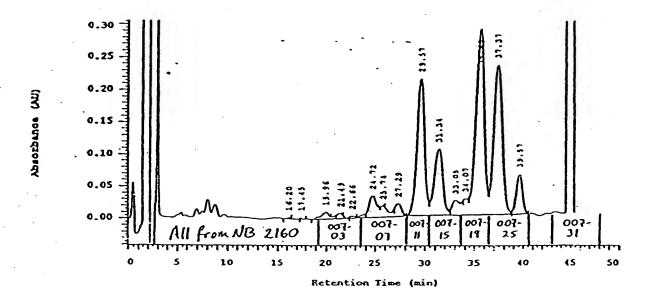
HPLC separation of the constituents in F094

FIG 25



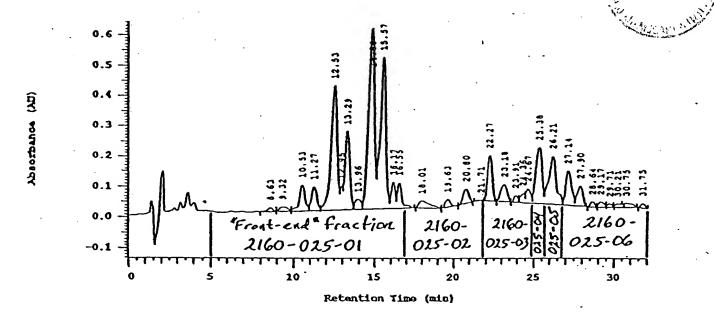
HPLC separation of the constituents in F035

FIG 26



. First Fractionation by Semi-Prep HPLC of F094

FIG 27



Second Fractionation by Semi-Prep HPLC of F094

FIG 28

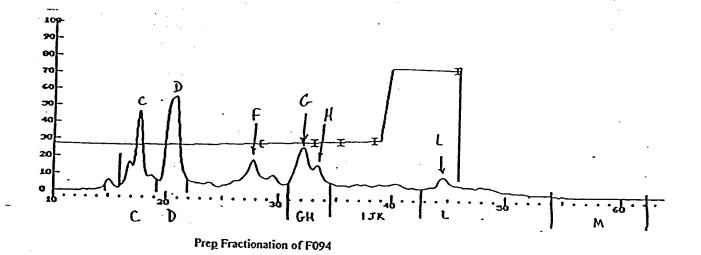


FIG 29

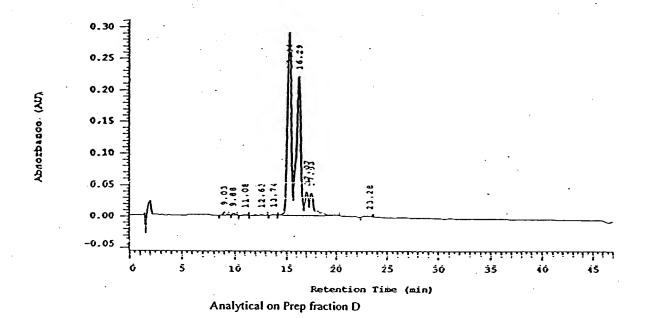


FIG 30

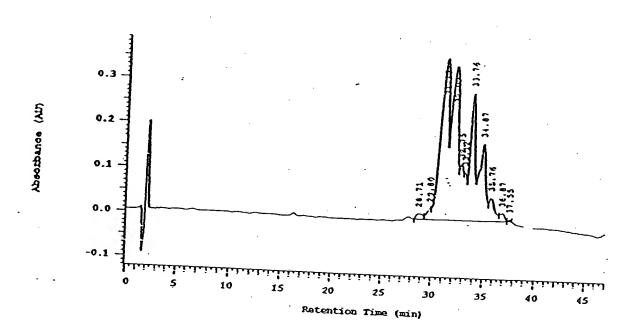
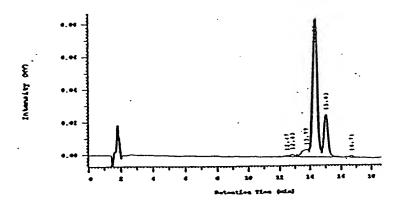


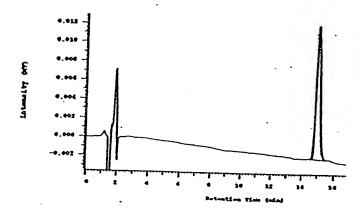
FIG 31

Analytical on Prep fraction G/H



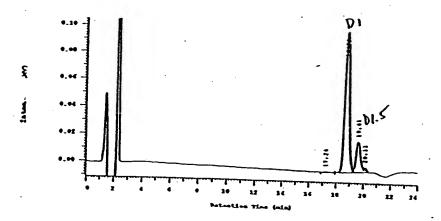
. G1 after second PFP column purification.

FIG 32



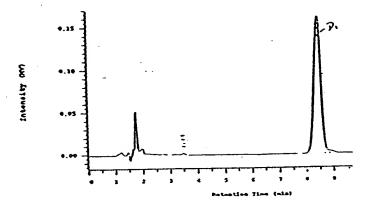
G1 after final C-18 purification

FIG 33



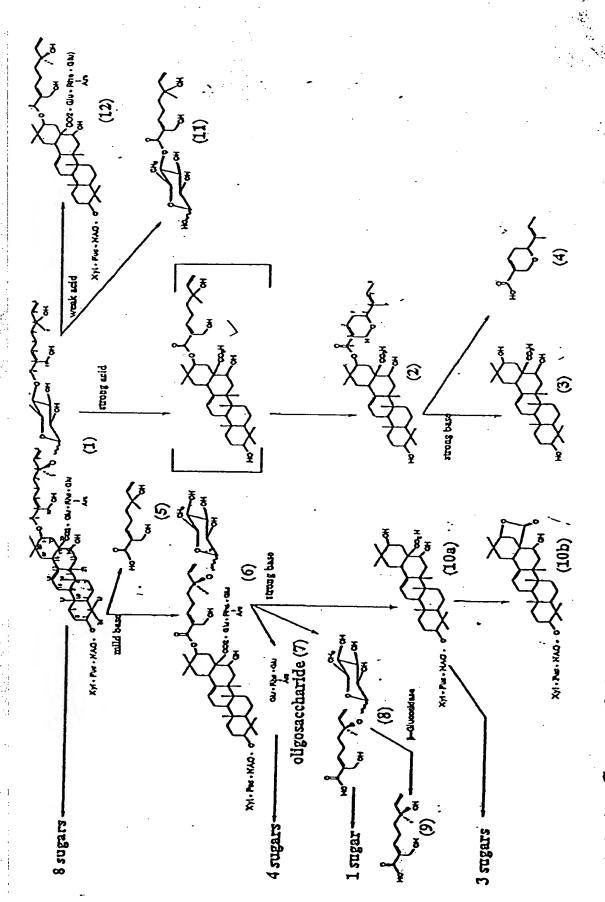
DI after Waters C-18 column purification.

FIG 34

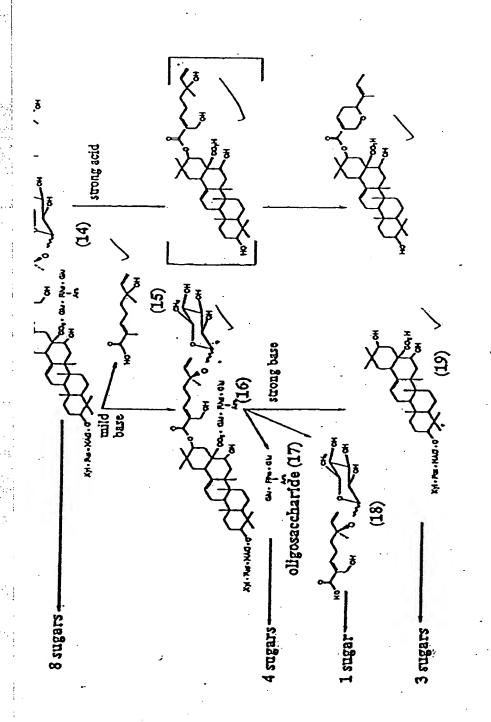


D1 after final C18-Aq purification

FIG 35

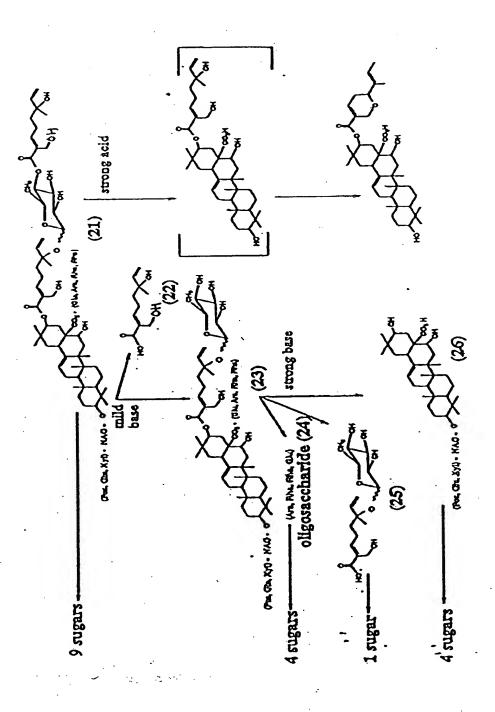


Compounds from the Degradation of D1



· Compounds from the Degradation of G1

用6.3%

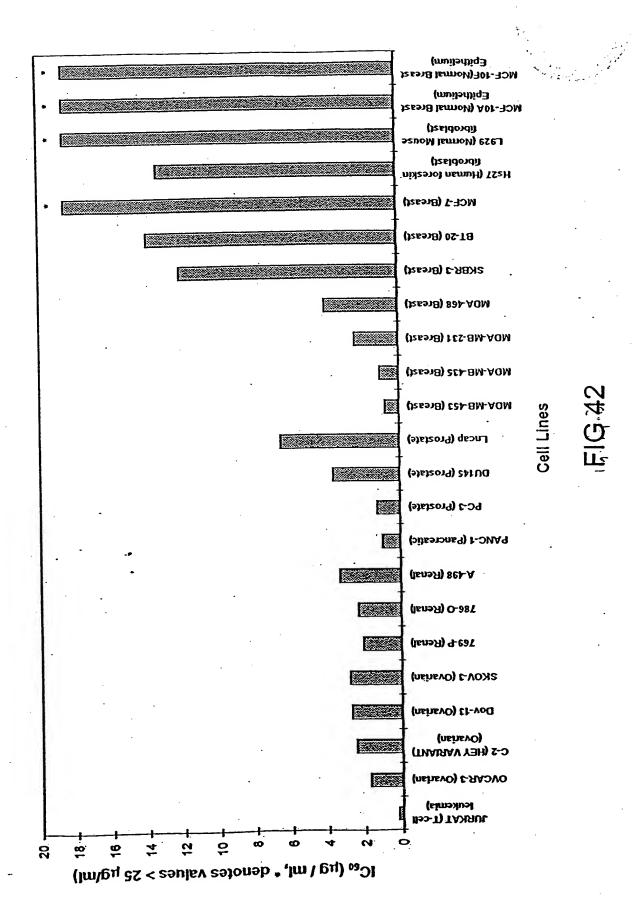


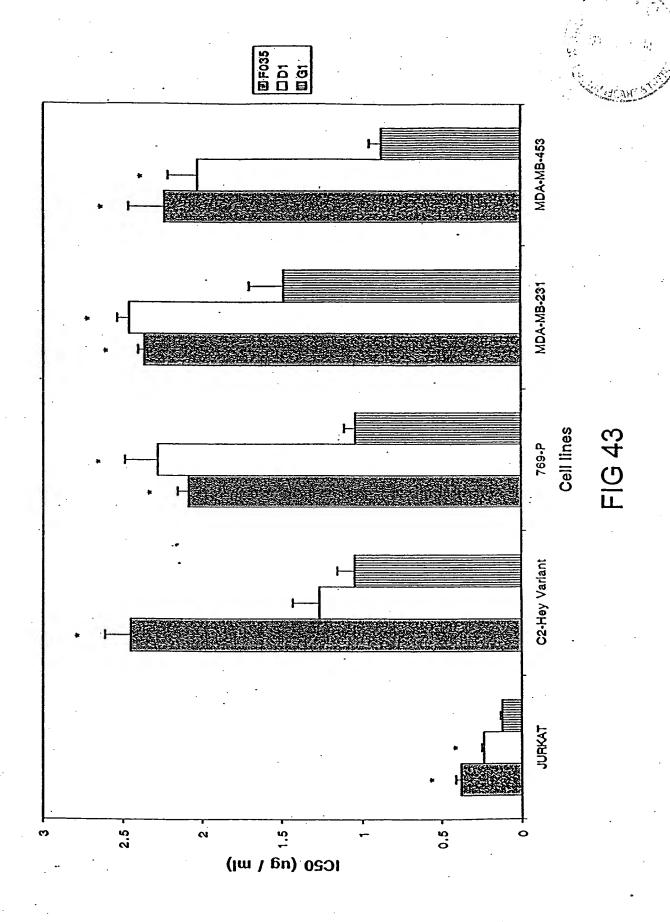
Compounds from the Degradation of B1

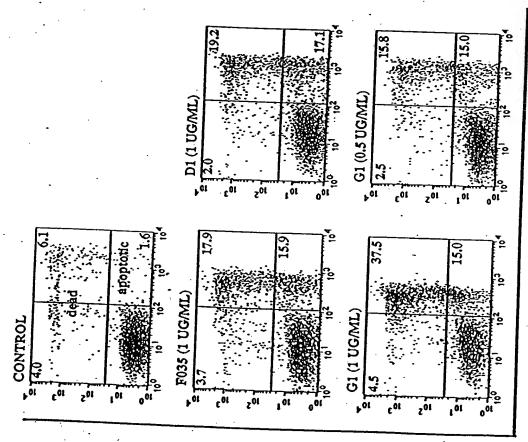
FIG. 39

FIG. 40

FIG. 41



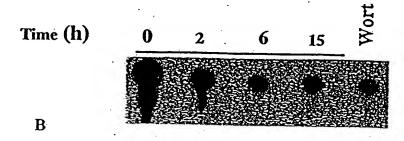




Ы

The second secon

Fraction 35 treatment



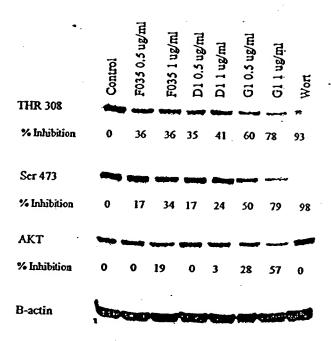
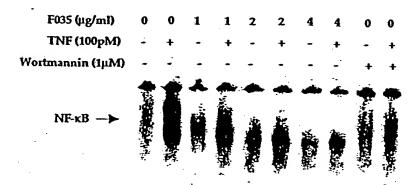


FIG 45,5

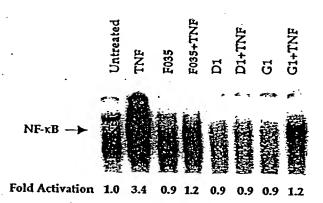
A



Fold Activation

1.0 3.9 1.1 1.7 1.2 1.5 0.9 1.1 1.0 1.1

B



CO SOS Untreated LPS F035-LPS Wortmannin Wortmannin

SON!
PHA+PMA
F035
F035
F035
F035

FIG 46

Effect of F035 & D1 on cleavage of PARP in Jurkat cells.

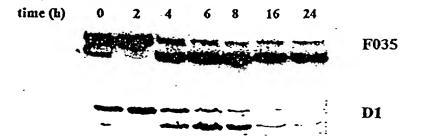


FIG 47

Effect of z-vad fmk on F035 induced PARP cleavage in Jurkat cells

F035 - + - + z-vad fmk - - + +

Effect of F035, F094, D1 & G1 on caspase activity in Jurkat cells.

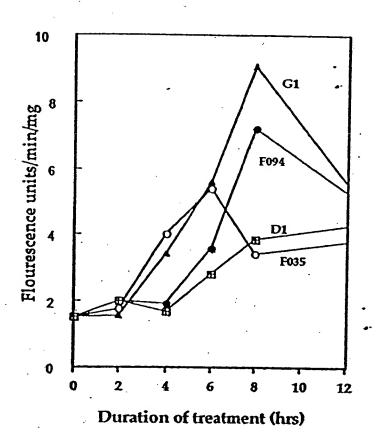
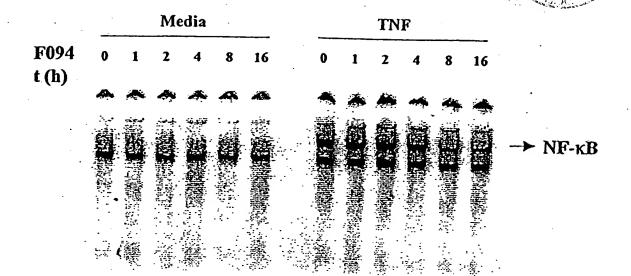


FIG 49

Effect of F035 on cytochrome c release from Jurkat mitochondria



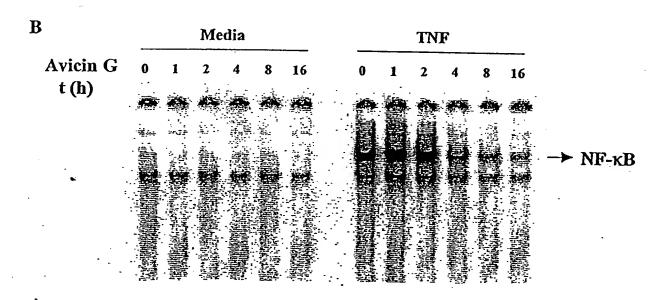
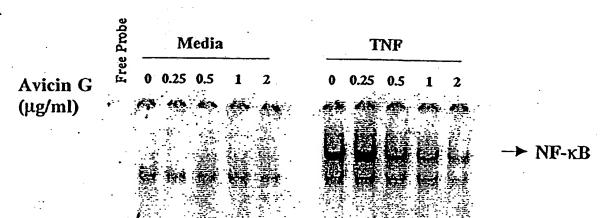
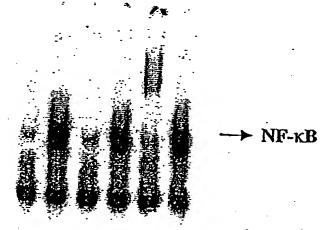


FIG. 51 A-B

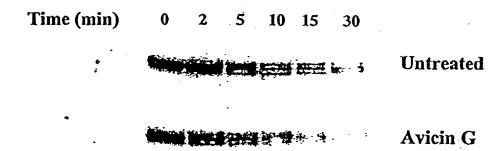
A



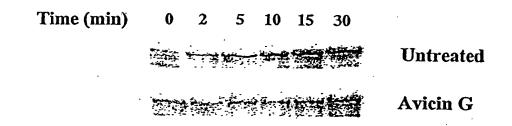
B

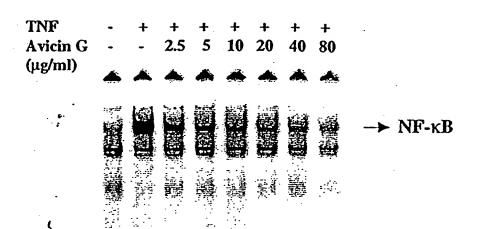


A IKB



B p65

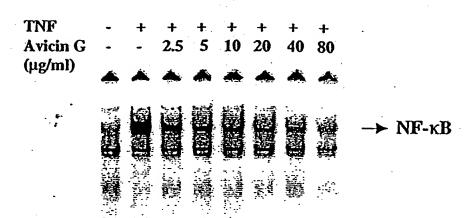




B

ſ

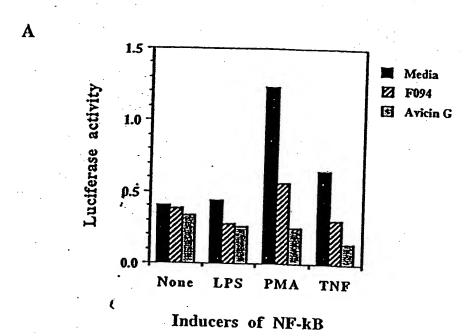


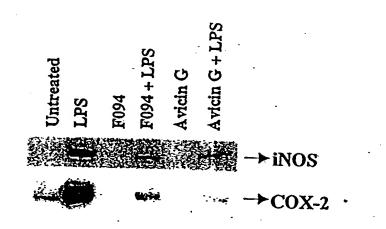


В

C

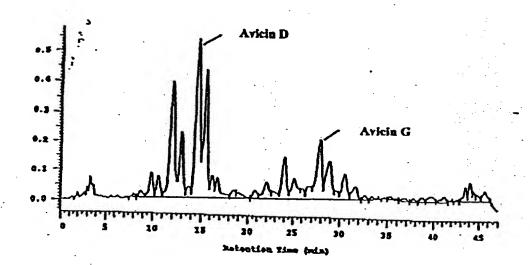






B

FIG. 55 A, B



ICso Values

HPLC Separation of the Avicins in F094

0.331-0.407 µg/ml

0.320-0.326 µg/ml

0.160-0.181 µg/ml

Avicia G

Annexin-V positive cells (%)

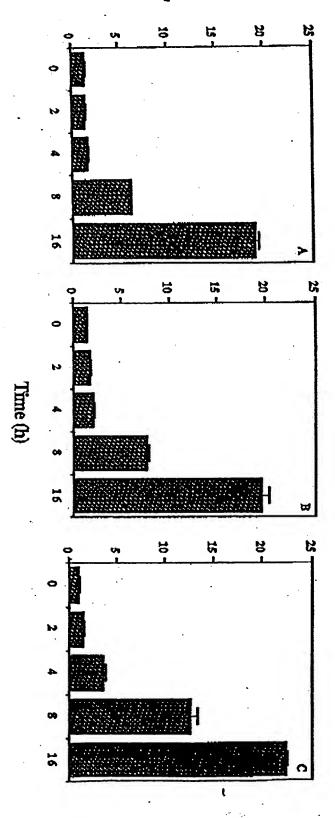


FIG. 57

Time (h) 0 0.5 1 2 4



Mixture

Fold increase

1.0 0.8 0.8 1.3 1.5



Avicin D

Fold increase

1.0 1.5 1.7 1.9 3.5



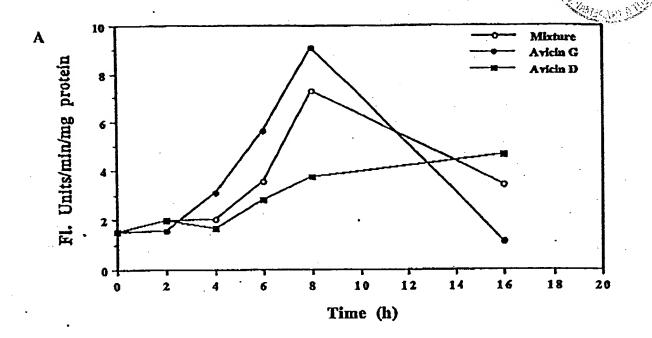
Avicin G

Fold increase

1.0 3.5 4.7 6.3 8.4

A

C



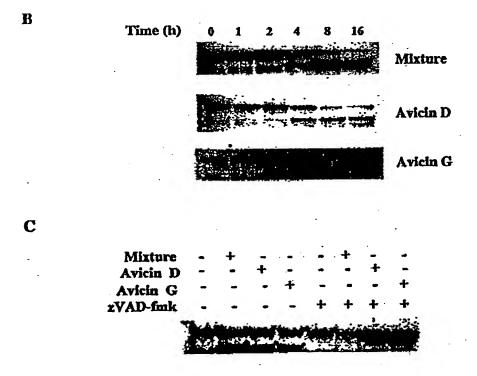
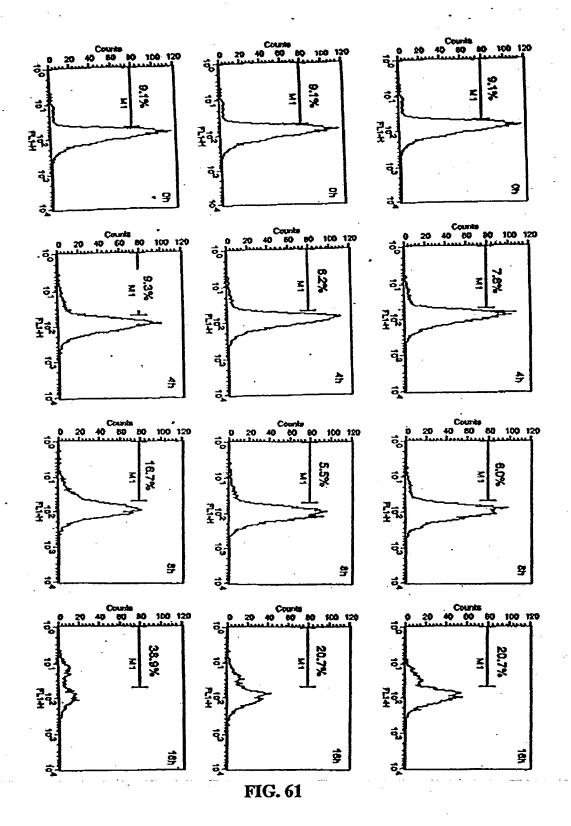
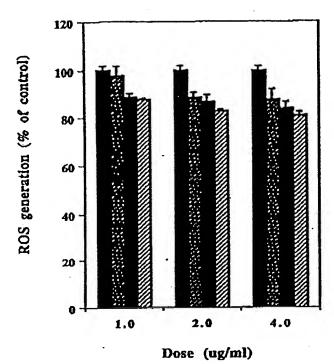


FIG. 60





Untreated

- Avicins (mixture)
- Avidn D
- 🖾 Avicia G

FIG. 62

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